REMARKS

Claims 1-25 were pending in this case. Applicants thank the Examiner for considering the Applicants' response to the restriction requirement filed May 12, 2003. The Examiner has maintained the restriction of claims 1-25 and has withdrawn non-elected claims 14-25. Applicants cancel withdrawn claims 14-25 without prejudice and reserve the right to pursue the subject matter of these claims in this or a continuing application. Accordingly, claims 1-13 are currently pending and have been rejected. Applicants respectfully request consideration and examination of this application and the timely allowance of the pending claims in view of the arguments below.

Anticipation Rejection Under 35 USC § 102

Claims 1-3 and 7-9 are rejected under 35 USC 102(b) as allegedly being anticipated by U.S. Patent No. 4,522,826 to Sunshine *et al.* (hereafter "*Sunshine*"). In particular, the Examiner contends that the recitation of an intended formulation would be an inherent property of the prior art composition in *Sunshine*.

A proper anticipation rejection requires that each and every limitation of the claimed invention be disclosed in a single prior art reference. Further, to serve as an anticipation reference in an inherency rejection, the reference must make clear that the missing descriptive matter is necessarily present in the thing described in the reference. *Schering Corporation v. Geneva Pharmaceuticals, Inc.*, 339 F.3d 1373, 1376 (Fed. Cir. 2003).

Applicants respectfully traverse this rejection and address the teachings of *Sunshine* below.

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Claim 1 of the instant invention is directed to a composition comprising ibuprofen and diphenhydramine in an amount effective to treat a pain-related disturbance, where such a composition is *formulated to prevent negative interactions between the diphenhydramine and the ibuprofen*. It appears that the Examiner has failed to take this limitation of the claimed invention into consideration. *Sunshine* does not disclose the claimed compositions, expressly or inherently. *Sunshine* specifically fails to disclose this limitation of the claimed invention, where the composition is formulated to prevent negative interactions between ibuprofen and diphenhydramine.

Specifically, *Sunshine* discusses a prophetic composition comprising an analgesic/anti-inflammatory agent such as, for example, ibuprofen (*see* column 6, lines 39-50), and a sleep-inducing agent such as diphenhydramine (*see* column 7, lines 46-60). Further, Example 1 of *Sunshine* discusses administration of solutions or suspensions of ibuprofen and/or diphenhydramine to mice via gavage, and an enhanced analgesic effect in mice upon administration of these compounds. There is no teaching or suggestion in *Sunshine*, however, of an orally administrable composition which comprises *both* ibuprofen and diphenhydramine. *Sunshine* only discusses administration of combinations of separate doses of ibuprofen and diphenhydramine to mice via gavage. *See*, for example, column 10, Table 2.

The claimed invention is directed to formulations that are created to prevent undesirable negative interactions between ibuprofen and diphenhydramine and include, for example, pharmaceutical formulations, such as, bilayer tablets and soft gelatin capsule containing polyethylene glycol. (*See*, for example, pages 12-14 of the specification as filed). The bilayer tablets or caplets of the instant invention physically

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separate ibuprofen and diphenhydramine, thereby preventing any negative interactions between the two compounds. The present invention also solves the problem associated with negative interactions between diphenhydramine hydrochloride and ibuprofen by using soft gelatin capsules containing these compounds in combination with polyethylene glycol, which is believed to protect against this interaction.

The Examiner points to column 8, lines 4-10 of *Sunshine*, as teaching that the composition disclosed in *Sunshine* may be formulated as a layered tablet. Applicants submit that *Sunshine*, however, discloses layered tablets where each layer contains both ibuprofen *and* diphenhydramine. *See*, column 8, line 4 of *Sunshine*, stating "one layer may contain an initial dosing amount of, for example, ibuprofen, of 400 milligrams and 25 milligrams of diphenhydramine, whereas two or more further layers may contain, for instance, 100 milligrams of ibuprofen and 15 to 25 milligrams of diphenhydramine." Applicants submit that the layered tablets described in *Sunshine* (*see* column 8, lines 6-13), which contain ibuprofen and diphenhydramine in the same layer, are not expected to prevent negative interactions between ibuprofen and diphenhydramine.

In light of the above arguments, Applicants submit that it is clear that *Sunshine* does not teach, contemplate, or even suggest compositions comprising ibuprofen and diphenhydramine, where the compositions are formulated to prevent negative interactions between the two compounds. *Sunshine* does not even recognize this problem. Therefore, the *Sunshine* composition is not formulated to prevent any negative interactions between ibuprofen and diphenhydramine.

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Accordingly, Applicants submit that *Sunshine* does not anticipate the claimed invention, either expressly or inherently, and that claims 1-3 and 7-9 are in condition for allowance.

Obviousness Rejection Under 35 USC § 103(a)

Claims 4-6 and 10-12 are rejected under 35 USC § 103(a) as allegedly being obvious over *Sunshine*. In particular, the Examiner contends that it would be obvious to one of ordinary skill in the art to modify the composition of *Sunshine* to employ specific salts of diphenhydramine recited in the claimed invention (claims 10-12) or use specific pharmaceutical forms, e.g., caplets, gelatin capsules etc. (claims 4-6).

Although a prior art device may be capable of being modified to run the way the apparatus is claimed, there must be a suggestion or motivation in the references to do so. *In re Mills*, 916 F.2d 680 (Fed. Cir. 1990); MPEP § 2143. 01. Applying this principle to the instant rejection, Applicants submit that *Sunshine* provides no suggestion or motivation to modify the composition disclosed in *Sunshine* as recited in instant claims 4-6 and 10-12.

Claims 4-6 are directed to a composition of ibuprofen and diphenhydramine formulated either as a bilayer tablet, a bilayer caplet or a soft gelatin capsule containing polyethylene glycol. Claims 10-12 are directed to compositions containing ibuprofen in combination with either diphenhydramine hydrochloride or diphenhydramine citrate, which are formulated to prevent negative interactions between the two compounds. It appears that the Examiner has failed to consider the limitation that the compositions of the claimed invention are formulated to prevent a negative interaction between ibuprofen and diphenhydramine.

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As discussed above, *Sunshine* fails to describe any compositions containing both ibuprofen and diphenhydramine that are formulated to prevent a negative interaction between the two compounds. *Sunshine* does not even recognize the interaction potential between ibuprofen and diphenhydramine.

The Examiner refers to column 1, lines 60-65 of *Sunshine* as teaching that diphenhydramine is commercially available as a hydrochloride salt. The Examiner also refers to column 7, lines 31-35 as teaching that polyethylene glycol is an acceptable carrier for the compositions of *Sunshine*.

Applicants submit that there are likely to be negative interactions between ibuprofen and diphenhydramine when they are contained in a standard tablet or caplet, including dissolution failures, eutectic formation and liquefaction, appearance problems (mottling and peeling), accelerated degradation and potential low potency (active ingredients being lost in the formulation process). These negative interactions are especially pronounced when diphenhydramine hydrochloride is combined with ibuprofen. *See,* page 12, lines 17-18, of the specification as filed. For example, a 50:50 composition of diphenhydramine hydrochloride and ibuprofen when taken from a dry to a wet state results in a transformation from a white powder to a translucent gray sticky mass even after it was dried again, with the change in opacity and color indicating that a chemical interaction had occurred. *See*, page 12, line 19 to page 13, line 6 of the specification as filed. The present invention solves the problem associated with negative interactions between diphenhydramine hydrochloride and ibuprofen by using soft gelatin capsules containing these compounds in combination with polyethylene glycol, which is believed to prevent against this interaction.

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Therefore, while *Sunshine* discusses that diphenhydramine hydrochloride is commercially available, *Sunshine* fails to provide any suggestion to modify its combinations to use a hydrochloride salt of diphenhydramine. Further, even if *Sunshine* suggested the use of diphenhydramine hydrochloride in combination with ibuprofen, such a combination would be undesirable, absent further steps taken to prevent an interaction between diphenhydramine hydrochloride and ibuprofen. Further, *Sunshine* merely discusses use of polyethylene glycol as a binder in a laundry lists of other binders, many of which we believe would not prevent this negative interaction. *See*, column 7, lines 30-33. There is no suggestion or teaching in *Sunshine*, however, of using polyethylene glycol in combination with ibuprofen and diphenhydramine in soft gelatin capsules in order to prevent the negative interaction, as recited in the instant claims. Thus, Applicants submit that there is no motivation or suggestion in *Sunshine* of the desirability of modifying its teachings to arrive at the claimed invention.

In view of the foregoing, Applicants submit that claimed invention is not obvious in view of the cited art and that claims 4-6 and 10-12 are in condition for allowance.

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CONCLUSION

In view of the foregoing remarks, Applicants respectfully request withdrawal of this rejection and timely allowance of the pending claims. Should the Examiner have remaining questions or concerns regarding this application, Applicants request that the Examiner contact the undersigned at 202-408-4086 to schedule an interview to discuss the application.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: January 20, 2004

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